

### **REMARKS**

Upon entry of the foregoing amendments, allowed claims 33, 34 and 49-52, 54, 55 and 57-61 will be pending. Claims 33, 59, 60 and 61 are the only pending independent claims.

Only claim 61 has been rejected and in view of the foregoing amendment, Applicants respectfully but urgently submit that claim 61 is now allowable, such that this application is now in full condition for allowance.

### **Explanation of and Support for the Amendments**

#### **Amendments to the Specification**

The specification has been amended to correlate the figure designations of the specification to the figure designations of the drawings as the drawings were amended in the present application in Amendments filed July 31, 2001 and June 30, 2002. These amendments take into consideration the Examiner's comments in item 3 of the Detailed Action portion of the Office Action of April 16, 2010 (Paper No. 20100411) in related U.S. Application No. 11/933,411. Since many of the figures comprise different portions, e.g. FIG. 14 comprises FIGS. 14A – 14G, where appropriate, the particular portions have been indicated where referenced elsewhere in the specification, rather than only in the Brief Description of the Figures and Tables section of the application.

The paragraph describing FIGS. 13A – 13C was revised to correct a few typographical errors.

Several paragraphs of the specification were previously amended in the present application on October 25, 2002, to delete the specific URL address per the Examiner's comments in item 2 of a Detailed Action portion of an Office Action of July 12, 2002, so as to only refer broadly to the World Wide Web, without providing any specific addresses. Also in view of the Examiner's comments in item 2 of the Detailed Action portion of the Office Action of April 16, 2010 (Paper No. 20100411) in related U.S. Application No. 11/933,411, these paragraphs were revised to delete any reference to the World Wide Web. The SIGCLEAVE program is a well known program available from a number of sources, including the Australian National Genomic Information Service (ANGIS) mentioned in the specification.

All of the amendments to the specification are supported by the application as filed and no new matter has been added. Accordingly, entry of the amendments to the specification and reconsideration and withdrawal of the objection to the specification and comments concerning the drawings are respectfully requested.

**Amendments to the Claims**

Claim 61 has been amended to read: An isolated protein having at least 90% sequence identity to SEQ ID NO:23 or SEQ ID NO:35, wherein one or more variable regions of a wild-type NhhA polypeptide are absent and wherein the isolated protein is immunogenic.

This is supported at least by the following locations of the application as filed:

Page 3, lines 21-24, which read as follows, relating to variable regions, that is, the non-conserved regions of the isolated protein (emphasis added):

It will be appreciated that according to this aspect, suitably one or more non-conserved amino acids of a variable region of an NhhA polypeptide, designated as V1, V2, V3 or V4 regions in FIG. 1, are deleted with respect to a wild-type NhhA polypeptide.

This is reinforced at page 11, lines 21-24, which read as follows (emphasis added):

Suitably, the polypeptides of the first aspect have at least a portion of one of the V1, V2, V3 or V4 regions deleted with respect to the corresponding wild-type sequence, and accordingly, may be collectively referred to as examples of “*deletion mutants*”.

Page 4, lines 15-18, specifically discloses that the first aspect of the invention includes homologs of the isolated protein.

Page 15, lines 11-13, specifically discloses that the homologs can have various degrees of identity, including 90% identity, as follows (emphasis added):

Polypeptide homologs share at least 70%, preferably at least 80% and more preferably at least 90% sequence identity with the amino acid sequences of modified NhhA polypeptides of the invention as hereinbefore described.

As noted in various locations throughout the application, for example in the Summary of the Invention (page 2, lines 18-24), after explaining that the NhhA surface antigen has variable and conserved regions, the application discloses:

The variable regions may be immunogenic and tend to elicit strain-specific immune responses, such that vaccines incorporating an NhhA antigen derived from a particular strain of *N. meningitidis* tend to preferentially immunize against that particular strain. As a result, the present inventors have sought to produce a modified NhhA polypeptide which elicits an immune response which is not as strain-specific as that elicited by wild-type NhhA.

Thus, the amendment to claim 61, covering an isolated, immunogenetic modified NhhA where one or more variable regions are absent is fully supported by the application as filed, its entry is respectfully requested.

Claim 61, prior to the present amendment, was rejected on the grounds of obviousness over Peak et al. WO 99/31132 ("Peak"). As understood, the Examiner took the position that since Peak discloses variants of wild-type NhhA proteins, such variants are not wild-type sequences. Moreover, where the variants can be homologs, including 90% homologs of proteins having a SEQ ID NO:5, not only does Peak teach proteins that are not wild-type proteins, but also, it would have been obvious to one skilled in the art at the time of the invention (now more than ten years ago) to isolate and use a modified NhhA protein that has at least 90% to a protein having SEQ ID NO:23 or 35. Applicants respectfully traverse this rejection.

Applicants recognize that in an obviousness determination, there is some degree of hindsight needed, in that without knowing what an applicant claims to be his or her invention, an Examiner cannot perform a reasonable search and examination. However, in this case, the Examiner has gone too far with respect to hindsight reconstruction of the invention as claimed in even previously pending claim 61, since one skilled in the art, without undue experimentation in view of the teaching of Peak would not have been able to determine which of the amino acids to remove or change from the wild type NhhA SEQ ID NO:5 of Peak, to produce a homolog having at least 90% sequence identity to the non-wild-type SEQ ID NOs: 23 or 35 of the present invention.

In view of the currently amended claim 61, any asserted obviousness is even a further stretch. Thus, now claim 61 recites that respectfully submit that it, in prior responses, have

pointed out that “one or more variable regions of a wild-type NhhA polypeptide are absent” in the isolated protein.

Peak does not disclose or even suggest the concept that the “variant” may exclude one or more entire variable regions of any of the exemplary wild-type or other proteins disclosed in Peak. Thus, “variant” is defined as follows in Peak at page 11, lines 22-24: The term “variant” refers to polypeptides in which one or more amino acids have been replaced.” Then Table 1 provides a list of conservative amino acid substitutions and thereafter is a brief disclosure of certain other non-conservative amino acid substitutions, which leads to a brief discussion of the homology of the variants. Nowhere does Peak enable anyone skilled in the art at the time of the invention to understand, let alone obviously eliminate one or more variable regions of an isolated protein having a SEQ ID NO:23 or 35, such that the isolated protein would not have one or more variable regions of a wild-type NhhA polypeptide. This disclosure or even a hint or suggestion of such a disclosure is plainly not present in Peak.

In view of this even further distinction of the subject matter of claim 61 over Peak, Applicants respectfully request reconsideration and withdrawal of the obviousness rejection.

Applicants respectfully submit that the present application is now in full condition for allowance and an early Notice of Allowance of all pending claims is respectfully solicited.

Respectfully submitted,

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(Date)

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